

## Development of a Chondrogenic Drug Candidate Targeting Cartilage-residing Mesenchymal Stem Cells for the Treatment of Osteoarthritis

### Grant Award Details

Development of a Chondrogenic Drug Candidate Targeting Cartilage-residing Mesenchymal Stem Cells for the Treatment of Osteoarthritis

**Grant Type:** Preclinical Development Awards

**Grant Number:** PC1-08142

**Project Objective:** This project is developing a small molecule therapy to be injected intra-articularly to treat osteoarthritis. The project is completing process development activities to scale their manufacturing to a GMP-compatible process, complete GMP manufacturing, and perform in vitro and in vivo IND-enabling studies. The CLIN1 award running in parallel to this is funding the pivotal IND-enabling GLP toxicology studies, but all other remaining IND-enabling activities are funded under this award. The project is moving nicely towards their objective of an IND filing in Q3 of this year.

#### Investigator:

<b>Name:</b>	Peter Schultz
<b>Institution:</b>	California Institute for Biomedical Research
<b>Type:</b>	PI

<b>Name:</b>	Shoutian Zhu
<b>Institution:</b>	California Institute for Biomedical Research
<b>Type:</b>	Co-PI

**Disease Focus:** Bone or Cartilage Disease

**Human Stem Cell Use:** Adult Stem Cell

**Award Value:** \$2,306,703

**Status:** Closed

### Progress Reports

**Reporting Period:** Year 1

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## Grant Application Details

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<b>Application Title:</b>	Development of a Chondrogenic Drug Candidate Targeting Cartilage-residing Mesenchymal Stem Cells for the Treatment of Osteoarthritis
<b>Public Abstract:</b>	<p>Osteoarthritis (OA) is the most prevalent musculoskeletal disease affecting nearly 27 million people in the United States, and is the leading cause of chronic disability in the United States. Current therapeutic options are limited to pain or symptom-modifying drugs and joint replacement surgery; no disease-modifying drugs are approved for clinical use. OA is characterized by progressive degeneration of the articular cartilage, resulting from abnormal activation, differentiation and death of cartilage cells. A unique and unexplored therapeutic opportunity exists to induce somatic stem cells to regenerate the damaged tissue and reverse the chronic destructive process. Cartilage contains resident mesenchymal stem cells (MSCs) that can be differentiated in vitro to form chondrocytes. This observation suggests that intra-articular injection of a small molecule that promotes chondrogenesis in vivo will preserve and regenerate cartilage in OA-affected joints. Targeting resident stem cells pharmacologically also avoids the risks and costs associated with cell-based approaches. In previous preclinical studies we have identified a small molecule drug candidate that specifically induces chondrocyte differentiation in culture and improves cartilage repair in OA animal models. In the proposed study we will optimize the regimen for dose, frequency and duration. We will also profile the preclinical candidate (PCC) for physicochemical, pharmacological and toxicological properties, draft a detailed plan for phase 1 clinical trial, and prepare documents and conduct a pre-IND meeting with the FDA. If successful, we will initiate IND-enabling studies and subsequent phase 1 clinical trial for the PCC.</p>
<b>Statement of Benefit to California:</b>	<p>Osteoarthritis (OA) is the most prevalent musculoskeletal disease and globally the 4th leading cause of Years Lost to Disease (YLD). OA affects over 40 million Americans and the magnitude of the problem is predicted to increase even further with the obesity epidemic and aging of the baby boomer generation. It is estimated that 80% of the population will have radiographic evidence of OA by age 65 years. The annual economic impact of arthritis in the U.S. is estimated at over \$100 billion, representing more than 2% of the gross domestic product. OA accounts for 25% of visits to primary care physicians. In 2004 OA patients received 650,000 knee and hip replacements at a cost of \$26 billion. Without change in treatment options 1.8 million joint replacements will be performed in 2015. OA is a painful, degenerative type of arthritis; physical activity can become difficult or impossible. Some patients with osteoarthritis are forced to stop working because their condition becomes so limiting. OA can interfere with a patient's ability to even perform routine daily activities, resulting in a decrease in quality of life. The goals of osteoarthritis treatment are to relieve pain and other symptoms, preserve or improve joint function, and reduce physical disability. Current therapeutic options are limited to pain medications and joint replacement for patients with advanced disease. No disease-modifying OA drugs are approved for clinical use. OA is thus a major unmet medical need with a huge clinical and socioeconomic impact and a complete absence of effective therapies. Clearly the development of a new therapeutic that is both symptom and disease modifying would have a significant impact on the well-being of Californians and reduce the negative economic impact on the state resulting from this highly prevalent disease.</p>

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